

[illegible]

variable region encoding nucleic acids comprising an acceptor variable region framework containing donor CDRs and a plurality of different amino acids at one or more framework regions and CDR amino acid positions;

- 5 (c) coexpressing said populations of heavy and light chain variable region encoding nucleic acids to produce diverse combinations of heteromeric variable region binding fragments, and (d) identifying one or more heteromeric variable region binding fragments having
- 10 affinity substantially the same or greater than the donor CDR heteromeric variable region binding fragment. A method of optimizing the binding affinity of an antibody variable region is also provided. The method consists of: (a) constructing a population of antibody variable
- 15 region encoding nucleic acids, said population comprising two or more CDRs containing a plurality of different amino acids at one or more CDR amino acid positions;
- (b) expressing said population of variable region encoding nucleic acids, and (c) identifying one or more
- 20 variable regions having binding affinity substantially the same or greater than the donor CDR variable region. The variable region populations can be heavy or light chains and can be expressed as individual populations or they can be coexpressed to produce heteromeric variable
- 25 region binding fragments.